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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,159

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Jan Barnikov

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04/29/2009

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EXAMINER

PAK, YONG D

ART UNIT

PAPER NUMBER

1652

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/591,159	<b>Applicant(s)</b> BARNIKOV ET AL.	
	<b>Examiner</b> YONG D. PAK	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 9-37 is/are pending in the application.
- 4a) Of the above claim(s) 15-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-14 and 37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/3/2006</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application is 371 of PCT/EP05/50899.

The preliminary amendment filed August 30, 2006, amending claims 1, 4-7, 9-16, 19, 21-231, and 37, canceling claim 8, and amending the specification on page 1, has been entered. No new matter has been entered.

Claims 1-7 and 9-37 are pending. Claims 15-36 are withdrawn. Claims 1-7, 9-14, and 37 are under consideration.

### ***Election/Restrictions***

Applicant's election of Group I (claims 1-7, 9-30, and 37) with a further species election of the mutant human AGT consisting of the following modifications and properties:

Lys32Ile, Leu33Phe, Cys62Ala, Gin 115 Ser, Gin 116His, Lys 125Ala, Ala127Thr, Arg128Ala, Gly131Lys, Gly132Thr, Met134Leu, Arg135Ser, Cysl50G1y, Serl51G1y, Ser152Asp, Ala154Asp, Asn157Gly, Ser159Glu, truncation at 182

- (a) no detectable DNA interaction;
- (b) localization of the expressed protein in eukaryotic cells that is no longer restricted to the nucleus;
- (c) at least 1 O-fold improved expression yield as soluble protein and improved stability in E. coli;
- (d) improved stability under oxidizing conditions;

- (e) at least six-fold improved stability within cells after reaction with a substrate;
- (f) improved stability outside cells before and after reaction with a substrate; (g) at least four-fold increased in vitro solubility;
- (h) 45-fold higher reactivity against O6-alkylguanine substrates;
- (i) no detectable reactivity against DNA-based substrates; and
- (j) at least 10-fold reduced reactivity against Ng-substituted O6-alkylguanine substrates

in the reply filed on January 30, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 15-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 30, 2009.

Examiner notes that claims 16, 17, 19, 20, and 24 do not read on the elected species because the mutant of claims 16-17 and 19-20 does not have a Gly at position 150 and the mutant of claim 24 has a deletion of Leu34.

Examiner also notes that claims 9-14 are drawn to non-elected species. Only those encompassed by the elected species will be examined.

***Claim for Foreign Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on October 3, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers a new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 and 9-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 1-7 and 9-14, as written, do not sufficiently distinguish over mutant AGT as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products, such as being "isolated". Even though the claims are drawn to mutant AGT, such mutants can exist naturally. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v.*

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Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" as taught by the specification. See MPEP 2105.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 9-14 and claims 2-7 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9-14 refer to amino acids at specific positions or at the N or C-terminus". The metes and bounds of the claims are not clear. Since the claim does not recite the amino acid sequence of the wild type human AGT, it is not clear to the Examiner what amino acid residue in a given human AGT, is the amino acid "Cys62", or the "1 to 4 amino acids at the N-terminus or 1 to 40 amino acids at the C-terminus". This rejection can be overcome by providing a sequence identifier for the wild type human AGT.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-13, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Juillerat et al.

Claims 1-5, 9-13, and 37 are drawn to a fusion protein comprising a mutant of a wildtype human AGT, wherein said mutant has Pro140Phe, Asn157Arg, and Ser159Glu substitutions, wherein said fusion protein has (1) localization of the expressed mutant in eukaryotic cells that is no longer restricted to the nucleus, (2) improved expression yield or fivefold expression yield as soluble protein and improved stability in various host, such as E. coli, and (3) improved reactivity against O<sup>6</sup>-alkylguanine substrates.

Juillerat et al. (Chemistry & Biology Vol. 10, 2003 – form PTO-1449) discloses a fusion protein comprising a mutant of a wildtype human AGT fused to a GST protein, wherein said mutant AGT has Pro140Phe, Asn157Arg, and Ser159Glu substitutions (Table 1 on page 2). Examiner takes the position that the protein of Juillerat et al. inherently possesses the same material structure and functional characteristics as the enzyme of the instant invention since the protein of Juillerat et al. is (1) not restricted to the nucleus (page 3, right column), (2) fusion to the GST protein affords stability/solubility to the AGT mutant, (3) has improved reactivity against O<sup>6</sup>-alkylguanine substrates (Table 1), and (4) the Office does not have facilities for examining and comparing applicant's enzyme with the enzyme of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the fusion protein comprising the mutant AGT of the

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prior art does not possess the same material structure and functional characteristics of the claimed fusion protein comprising the mutant AGT). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. Therefore, the reference of Kusakabe et al. anticipates claims 1-5, 9-13, and 37.

### ***Examiner Comments***

Examiner notes that the elected species, as outlined above on page 2, is free of prior art. Therefore, examination of other withdrawn species of the Markush-type claim was extended. Since prior art was found that anticipates the Markush-type claim with respect to a *nonelected species*, the Markush-type claim was rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated by the prior art, the amended Markush-type claim will be reexamined.

### ***Conclusion***

Claims 1-7, 9-14, and 37 are rejected.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/

Primary Examiner, Art Unit 1652